# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

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| pplicant's or agent's file reference<br>1000PCT AWT/JML | **FOR FURTHER ACTION** | See Form PCT/IPEA/416 |
| ıternational application No.<br>**CT/AU2004/000865** | International filing date *(day/month/year)*<br>30 June 2004 | Priority date *(day/month/year)*<br>30 June 2003 |

ıternational Patent Classification (IPC) or national classification and IPC

ıt. Cl.[7] C12Q 1/68, C12M 1/34, G01N 33/48

.pplicant

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. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.

:. This REPORT consists of a total of 3 sheets, including this cover sheet.

;. This report is also accompanied by ANNEXES, comprising:

a. [X] *(sent to the applicant and to the International Bureau)* a total of **9** sheets, as follows:

- [ ] sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
- [ ] sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

b. [ ] *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or table related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

| | | |
|---|---|---|
| [X] | Box No. I | Basis of the report |
| [ ] | Box No. II | Priority |
| [ ] | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| [ ] | Box No. IV | Lack of unity of invention |
| [X] | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| [ ] | Box No. VI | Certain documents cited |
| [ ] | Box No. VII | Certain defects in the international application |
| [ ] | Box No. VIII | Certain observations on the international application |

| | |
|---|---|
| Date of submission of the demand<br>29 April 2005 | Date of completion of the report<br>11 July 2005 |
| Name and mailing address of the IPEA/AU<br>AUSTRALIAN PATENT OFFICE<br>PO BOX 200, WODEN ACT 2606, AUSTRALIA<br>E-mail address: pct@ipaustralia.gov.au<br>Facsimile No. (02) 6285 3929 | Authorized Officer<br>**BAYER MITROVIC**<br>Telephone No. (02) 6283 2164 |

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/AU2004/000865

Box No. I Basis of the report

With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

- ☐ international search (under Rules 12.3 and 23.1 (b))
- ☐ publication of the international application (under Rule 12.4)
- ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

With regard to the **elements** of the international application, this report is based on (*replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report*):

☐ the international application as originally filed/furnished

☒ the description:

pages **1, 2, 6, 8-21** as originally filed/furnished
pages* **3-5, 5A, 7** received by this Authority on **30 June 2005** with the letter of **30 June 2005**
pages* received by this Authority on with the letter of

☒ the claims:

pages as originally filed/furnished
pages* as amended (together with any statement) under Article 19
pages* **22-24, 24A** received by this Authority on **30 June 2005** with the letter of **30 June 2005**
pages* received by this Authority on with the letter of

☒ the drawings:

pages **1/3-3/3** as originally filed/furnished
pages* received by this Authority on with the letter of
pages* received by this Authority on with the letter of

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to the sequence listing (*specify*):

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/figs
- ☐ the sequence listing (*specify*):
- ☐ any table(s) related to the sequence listing (*specify*):

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Statement

| | | |
|---|---|---|
| Novelty (N) | Claims 1-13 | YES |
| | Claims | NO |
| Inventive step (IS) | Claims 1-13 | YES |
| | Claims | NO |
| Industrial applicability (IA) | Claims 1-13 | YES |
| | Claims | NO |

Citations and explanations (Rule 70.7)

The following documents identified in the International Search Report have been considered for the purposes of this report:

D1: US 2002/0136978
D2: WO 2000/25936
D3: WO 2001/15800
D4: WO 2003/031067

Document D1 discloses a method of in-situ synthesis of array of biopolymers on the patterned substrate to produce a diverse and addressable set of chemical compounds. Method is based on the electrostatic deposition of particles which are partially composed of nucleotides, amino acids, oligomers or similar compounds, which are charged by triboelectrification and which may carry charge controlling agents. Particles are first deposited onto an interim selectively charged substrate, which includes discrete areas with different charge. Interim substrate is a photoreceptor whose charge is changed by photo illumination to generate patterned regions with predetermined electrostatic charges. Particles carrying nucleotides and other moieties are present on the surface of the interim substrate, but they do not form the continuous functional layer.

Each of the remaining documents D2-D4 disclose a method of electrostatic deposition of charged particles onto a substrate which consists of patterned metal and dielectric layers to synthesize an array of oligomers or other compounds. A spatially resolved, addressable charge is formed onto the substrate in a predetermined manner. Chemical functionalities are present on the surface of the substrate. The use of photoconductors is not disclosed.

None of the above documents disclose the chemically functional layer providing a protective layer for photoconductive or dielectric layer and a chemically reactive surface for compounds deposited on the surface.

NOVELTY AND INVENTIVE STEP – CLAIMS 1-13

In light of the above observations it is concluded:
The subject matter of claims 1-13 is new and meets the requirements of Article 33(2) PCT with regard to novelty.
The claimed invention is also not obvious in the light of any of the cited documents nor is it disclosed in any obvious combination of them. It is also considered that it would not be obvious to a person skilled in the art in the light of common general knowledge either by itself or in combination with any of these documents. Therefore the subject matter of these claims is not obvious and meets the requirements of Article 33(3) PCT with regard to inventive step.

Selective de-protecting by direct light activated chemistry or photo-removable de-protecting techniques has been developed but these are somewhat inefficient resulting in short solid phase oligodeoxynucleotides, 20 to 25 nucleotides in length, in rather large unit feature sizes of 10 to 50 microns and it is an object of this invention to provide a more efficient chemical de-protecting process.

The applicant has surprisingly found that by the use of electrically charged emulsions which include the chemical de-protecting agent in the discontinuous phase and which are selectively deposited on predefined areas of a planar or other shaped substrate under the influence of an electric field, then more accurate, localised and efficient de-protecting may be possible.

BRIEF DESCRIPTION OF THE INVENTION

In one form therefore, the invention is said to reside in a substrate adapted for combinatorial chemistry, the substrate having;

a support;

a conductive layer on the support;

a dielectric layer of a material which will hold an electric charge; and

a chemically functional layer, the chemically functional layer providing a protective layer for the dielectric layer and a chemically reactive surface for compounds deposited on the surface;

whereby electrostatic charge patterns may be formed in a selected array upon or in the substrate.

In a further form the invention is said to reside in a substrate adapted for combinatorial chemistry, the substrate having;

a support;

a conductive layer on the support;

a photoconductive layer of a material upon which is adapted to have an electrostatic charge thereon selectively dissipated upon receiving incident radiation; and

a chemically functional layer, the chemically functional layer providing a protective layer for the photoconductive layer and a chemically reactive surface for compounds deposited on the surface;

whereby electrostatic charge patterns may be formed in a selected array upon the substrate to influence the movement of charged droplets in a liquid medium on the substrate.

In a further form the invention is said to reside in a substrate adapted for combinatorial chemistry, the substrate having;

a support;

a conductive layer on the support;

a photoconductive layer of a material which is adapted to have an electrostatic charge thereon selectively dissipated upon receiving incident radiation; and

a chemically functional layer, the chemically functional layer providing a protective layer for the photoconductive layer and a chemically reactive surface for compounds deposited on the surface;

whereby electrostatic charge patterns may be formed in a selected array upon the substrate to influence the movement of charged droplets in a liquid medium on the substrate.

In an alternative form the invention may be said to reside in a substrate adapted for manufacture of DNA arrays, the substrate having;

a support;

a conductive layer on the support;

a photoconductive layer of a material which is adapted to have an electrostatic charge thereon dissipated upon receiving incident radiation; and

a chemically functional layer, the chemically functional layer providing a protective layer for the photoconductive layer;

whereby electrostatic charge patterns may be formed in a selected array upon the substrate to influence the movement of charged droplets in a liquid medium on the substrate;

the chemically functional layer comprising at least in part a chemically active material to which a binder molecule can be attached, whereby a selected electric charge pattern may be generated upon the substrate by incident radiation to enable selective chemical de-protection of the binder molecules or DNA oligomers already joined to a binder molecule and application of nucleotides to selected binder molecules or to DNA oligomers already joined to a binder molecule.

In an alternative form the invention may be said to reside in a substrate adapted for manufacture of DNA arrays, the substrate having;

a support;

a conductive layer on the support;

a photoconductive layer of a material which is adapted to have an electrostatic charge thereon selectively dissipated upon receiving incident radiation; and

a chemically functional layer, the chemically functional layer providing a protective layer for the photoconductive layer;

whereby electric charge patterns may be formed in a selected array upon the substrate to influence the movement of charged droplets in a liquid medium on the substrate; the chemically functional layer providing a surface to which a binder molecule can be attached.

The support may be selected from a metal, glass, ceramic, or polymeric material and the support can be either clear or opaque and either flexible or rigid.

The incident radiation may be provided from either the front or rear of the substrate.

In a preferred embodiment the conductive layer may be combined with the support.

The conductive layer may be a very thin layer and may be transparent.

The conductive layer may be vacuum-deposited onto the support.

The conductive layer may be selected from a sputtered layer of metal or indium tin oxide, or a carbon nano-tube layer.

The dielectric or photoconductive layer of material which retains an induced electric charge may be an active layer and the charge on this layer may be influenced by radiation selected from infrared, visible, ultraviolet or x-ray.

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As discussed above the photoconductor surface has a chemically functional layer applied to it and this chemically functional layer may provide the surface for chemical functionalisation of the substrate, such that deposition and/or covalent chemistry can be undertaken on its surface. Depending on the nature of the photoconductor the chemically functional layer may range in thickness from mono-molecular to fractions of a millimetre.

The chemically functional layer may be adapted to prevent access or reaction between the liquids or reagents in the emulsion and other liquids used in the process and components of the dielectric or photoconductive layer. Alternatively or in addition the chemically functional layer may be a reactive material which allows a chemical reaction with another compound at its surface to form a derivatised or functionalised surface for subsequent reaction such as with linker molecules. Alternatively the chemically functional layer may be intrinsically reactive and provide a binder function.

The chemically functional layer may be formed from a silane, silicon dioxide, silicon nitride ($Si_xN_y$), titanium dioxide, Tyzor™, cross-linked or partially cross-linked epoxy novolac resin, polymerised oligomers, cross-linked resins, functionalised parylene (a polymer of di-para-xylyene with one or more functional groups), acrylates and methacrylates which may include functional groups, multi-functional acrylate and methacrylate monomers, monomers which have been cross-linked with a photo-initiator and the like. Multi-functional acrylate and methacrylate monomers refers to monomers with a plurality of double bonds. The functional group may be an active ester, epoxy, aromatic, acid, aliphatic and hydroxyl or the like.

Formation of the chemically functional layer may be achieved using several processes, including immersion of the substrate in reactive chemicals, "painting", dip-coating, spin-coating, vacuum deposition and vapour phase deposition, wherein the chemically functional layer becomes attached by covalent bonding or by other

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A substrate adapted for selective micron and nanometer scale deposition, the substrate having;

a support;

a conductive layer on the support;

a dielectric layer of a material which will hold an electrostatic charge; and

a chemically functional layer, the chemically functional layer providing a protective layer for the dielectric layer and a chemically reactive surface for compounds deposited on the surface;

whereby electrostatic charge patterns may be formed in a predetermined manner upon or in the substrate.

2. A substrate as in Claim 1 wherein the support is selected from the group comprising a metal, glass, ceramic, or polymeric material and the support is clear or opaque and flexible or rigid.

3. A substrate as in Claim 1 wherein the conductive layer is combined with the support.

4. A substrate as in Claim 1 wherein the conductive layer is a very thin layer and is transparent.

5. A substrate as in Claim 1 wherein the conductive layer conductive layer is vacuum-deposited onto the support.

6. A substrate as in Claim 1 wherein the conductive layer is selected from the group comprising a sputtered layer of metal or indium tin oxide, or a carbon nano-tube layer.

7. A substrate as in Claim 1 wherein the dielectric layer is selected from the group comprising a glass, a polymeric resin and a methylmethacrylate (MMA).

8. A substrate as in Claim 1 wherein the dielectric layer is a photoconductor.

9. A substrate as in Claim 8 wherein the photoconductor is selected from the group comprising zinc oxide, cadmium sulphide, lead sulphide, lead selenide, amorphous selenium, doped selenium, alloys of selenium including selenium-tellurium, selenium-arsenic, organic photoconductive materials including polyvinylcarbazole (PVK) and complexes of polyvinylcarbazole sensitised with trinitrofluorenone.

10. A substrate as in Claim 1 wherein the chemically functional layer is a material selected from the group comprising a silane polymer, silicon dioxide, silicon nitride ($Si_xN_y$), titanium dioxide, Tyzor™, cross-linked or partially cross-linked epoxy novolac resins, polymerised oligomers, cross-linked resins, functionalised parylene (a polymer of di-para-xylyene), acrylates and methacrylates which may include functional groups, multi-functional acrylates and methacrylates, monomers which have been crosslinked with a photoinitiator.

11. A substrate having;

a support;

a conductive layer on the support;

a photoconductive layer of a material which is adapted to have an electrostatic charge thereon selectively dissipated upon receiving incident radiation; and

a chemically functional layer, the chemically functional layer providing a protective layer for the photoconductive layer and a chemically reactive surface for compounds deposited on the surface;

whereby electrostatic charge patterns may be formed in a selected array upon the substrate to influence the movement of charged droplets in a liquid medium on the substrate.

12. A substrate adapted for manufacture of DNA arrays, the substrate having;
a support;
a conductive layer on the support;
a photoconductive layer of a material which is adapted to have an electrostatic charge thereon dissipated upon receiving incident radiation; and
a chemically functional layer, the chemically functional layer providing a protective layer for the photoconductive layer;
whereby electrostatic charge patterns may be formed in a selected array upon the substrate to influence the movement of charged droplets in a liquid medium on the substrate;
the chemically functional layer comprising at least in part a chemically active material to which a binder molecule can be attached, whereby a selected electric charge pattern may be generated upon the substrate by incident radiation to enable selective chemical de-protection of the binder molecules or DNA oligomers already joined to a binder molecule and application of nucleotides to selected binder molecules or to DNA oligomers already joined to a binder molecule.

13. A substrate adapted for manufacture of DNA arrays, the substrate having;
a support;
a conductive layer on the support;
a photoconductive layer of a material which is adapted to have an electrostatic charge thereon selectively dissipated upon receiving incident radiation; and
a chemically functional layer, the chemically functional layer providing a protective layer for the photoconductive layer;
whereby electric charge patterns may be formed in a selected array upon the substrate to influence the movement of charged droplets in a liquid medium on the

substrate; the chemically functional layer providing a surface to which a binder molecule can be attached.